FDA approves engineered cell therapy for treating rare sarcoma

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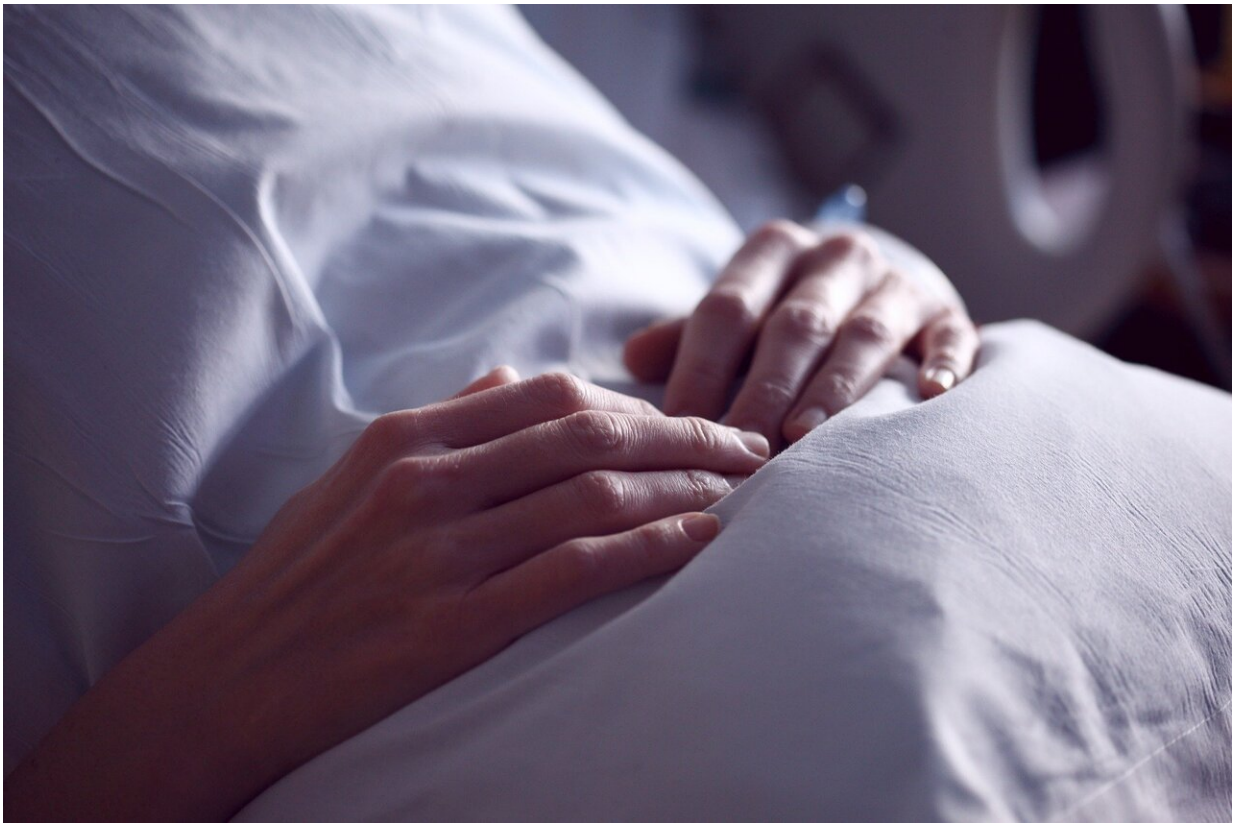

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The U.S. Food and Drug Administration (FDA) has granted accelerated approval for the immunotherapy afamitresgene autoleuecel (Tecelra, also known as afami-cel) for the treatment of adults with a rare soft

tissue cancer called synovial sarcoma.

Afami-cel is the first engineered T cell therapy to receive FDA approval for a solid tumor cancer.

The clinical trial that resulted in the drug's approval was led by Memorial Sloan Kettering Cancer Center (MSK) sarcoma specialist and immunotherapy expert Sandra D'Angelo, MD.

"This treatment offers an important new option for people with this rare cancer," Dr. D'Angelo says. "It is also an important step forward in the development of T cell therapies for solid tumors, which has been a major challenge."

Other cell therapies, such as chimeric antigen receptor (CAR) T cell therapy, involve targeting surface proteins to recognize and attack a cancer cell. Until now, these types of immunotherapies have been used only to treat blood cancers.

Using engineered cell therapies to treat solid tumors

Synovial sarcoma is diagnosed in fewer than 1,000 people in the United States every year. A cancer that can develop in the extremities or in the soft tissue in the abdomen or lung, it most often occurs in young adults. It is slightly more common in men than in women.

"Sarcoma in general, and synovial sarcoma in particular, is a type of cancer where more treatments are desperately needed," Dr. D'Angelo explains. "Once the disease spreads to other parts of the body, it is very difficult to control with the therapies we have now."

T cell receptor therapy targets solid tumors

Afami-cel is an engineered cell therapy, similar to the CAR T treatments that have been approved for treating certain blood cancers since 2017. With cell therapies, a patient's own T cells are collected from the blood and engineered in a lab to recognize cancer cells. They are then infused back into the bloodstream, allowing them to travel throughout the body to detect and destroy tumor cells.

Engineered cell therapies are often called "living drugs," and for many people with blood cancer, they have offered the hope of a cure.

Afami-cel is not a CAR T therapy but is in a related category called T cell receptor (TCR) therapy. The T cells are engineered to carry an extra tool that allows them to recognize proteins, or markers, that are hiding inside cancer cells. By contrast, CAR T therapies can only see these cancer markers when they are on the outside of tumor cells.

"With both CAR T and TCR therapies, you are giving the immune cells the ability to fight the cancer," Dr. D'Angelo explains. The cancer-causing protein that afami-cel targets is called MAGE-A4.

Another therapy that uses patients' own immune cells, known as TIL therapy, also recently received FDA approval for treating the solid tumor melanoma. TIL therapy requires that immune cells be extracted from tumors that are surgically removed and then expanded in the lab before being infused back into the patient.

Results of trial for rare soft tissue sarcomas

The Phase II clinical trial that resulted in the drug's approval was published in *The Lancet* in April 2024. Dr. D'Angelo was lead author of the paper, which reported that afami-celsignificantly shrank sarcoma tumors in more than one-third of patients.

"Some patients in the trial had their tumors completely disappear and have not had the cancer come back for several years," Dr. D'Angelo says.

The clinical trial was an international study that treated a total of 52 people who had been diagnosed with synovial sarcoma and myxoid/round cell liposarcoma (MRCLS), another type of soft tissue sarcoma. These patients had not responded to other therapies.

- Overall, almost 37% of patients saw their tumors shrink after receiving a single dose.
- The drug helped about 39% of people with synovial sarcoma and 25% of those with MRCLS.
- Patients with synovial sarcoma responded to this therapy for an average of 11.6 months, and those with MRCLS responded for an average of 4.2 months.

"These findings are significant for a group of patients who have largely exhausted other treatment options," Dr. D'Angelo says.

Side effects of afami-cel for sarcoma

Before receiving the cell therapy afami-cel, patients were first treated with chemotherapy. The most frequent side effect of that treatment was low blood counts.

About 71% of patients in the trial also experienced cytokine release syndrome (CRS), a common reaction after cell therapies. This occurs when the immune system temporarily goes into overdrive to fight the cancer. For most patients in the afami-cel trial, this syndrome was not severe.

Dr. D'Angelo hopes that eventually afami-cel may work against any type

of solid tumor that carries the mutated MAGE-A4 protein.

Afami-cel and other TCR therapies are also being studied in pediatric sarcomas.

More information: Sandra P D'Angelo et al, Afamitresgene autoleucel for advanced synovial sarcoma and myxoid round cell liposarcoma (SPEARHEAD-1): an international, open-label, phase 2 trial, *The Lancet* (2024). DOI: 10.1016/S0140-6736(24)00319-2

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